

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT PCT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference PHM.70582/WO	FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/GB00/03192	International filing date (day/month/year) 21/08/2000	Priority date (day/month/year) 27/08/1999
International Patent Classification (IPC) or national classification and IPC C07B37/10		
Applicant ASTRAZENECA AB		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.



2. This REPORT consists of a total of 7 sheets, including this cover sheet.

- ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☒ Certain documents cited
- VII ☒ Certain defects in the international application
- VIII ☒ Certain observations on the international application

Date of submission of the demand 23/02/2001	Date of completion of this report 09.08.2001
Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Herzog, A Telephone No. +49 89 2399 8033 

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/GB00/03192

I. Basis of the report

1. With regard to the **elements** of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17)*):

Description, pages:

1-9 as originally filed

Claims, No.:

1-8 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:
- ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/GB00/03192

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	7,8
	No:	Claims	1-6
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-8
Industrial applicability (IA)	Yes:	Claims	1-8
	No:	Claims	

2. Citations and explanations see separate sheet

VI. Certain documents cited

1. Certain published documents (Rule 70.10)

and / or

2. Non-written disclosures (Rule 70.9)

see separate sheet

VII. Certain defects in the international application

The following defects in the form or contents of the international application have been noted:
see separate sheet

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:
see separate sheet

Re Item V

Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

D1: XP004105664 (Spitzer, J.L. et al., Tetrahedron, vol. 53, no. 20 (1997), p. 6791-6808)

D2: XP002156524 (Smit, W.A., Tetrahedron Letters, vol. 27, no. 11 (1986), p. 1241-1244)

D3: XP002156525 (Simonian, S.O., Tetrahedron Letters, vol. 27, no. 11 (1986), p. 1245-1248)

- a) The present application does not meet the requirements of Article 33(2) PCT, because the subject-matter of present claims 1-6 is not new.

D1 discloses an alkyne cobalt carbonyl complex for the Pauson-Khand reaction which is polymer-supported. An alkynol of different chain length is used as the linker group between the cobalt carbonyl complex and the functionalised Merrifield's polymer beads (cf. abstract; page 6792, second §; page 6793, Scheme 1; page 6795, first scheme; page 6796, Scheme 2).

Due to the fact that in the present claims, the term "immobilised" is not further defined, D1 is novelty-destroying for present claims 1-6.

In D2 on page 1243, second §, it is mentioned that the reaction in Scheme 5 on said page, namely the Pauson-Khand conversion of the alkyne cobalt carbonyl complex 9a or 9b into the compound 10a or 10b, sharply accelerates if it is carried out not in solution, but in an absorbed state on the surface of an adsorbent such as SiO₂.

D3 also discloses the Pauson-Khand reaction with an alkyne cobalt carbonyl complex adsorbed on silicagel (cf. D3, abstract and page 1246, Scheme 1).

Again, due to the vague term "immobilised" used in the present claims, D2 and D3 are considered novelty-destroying for claims 1-6.

- b) The present application does not meet the requirements of Article 33(3) PCT because the subject-matter of present claims 1-8 does not involve an inventive

step for the following reasons:

1. The term "immobilised" is not clearly defined in the claims. Said feature is the only feature which could render the subject-matter claimed in the present application novel and inventive over the prior art. However, the claims do not explain how the invention could be carried out, and thus how the problem could be solved, contrary to the requirements of Articles 6 and 33(3) PCT.
2. According to claims 1, 2, 5 and 7, a transition metal carbonyl complex or alkyne transition metal carbonyl complex is used as a catalyst in the Pauson-Khand reaction. However, it is clear to the person skilled in the art that not all transition metal carbonyl complexes could be used in the Pauson-Khand reaction and thus solve the problem posed (Article 33(3) PCT).
3. In the example given in the description (cf. page 9), a catalyst A precursor resin has been used which contains cobalt as the transition metal (cf. scheme on page 4). No data is provided which could demonstrate that catalysts other than said catalyst A could be used to advantageously carry out the Pauson-Khand reaction and thus solve the problem posed (Article 33(3) PCT). The process using a heterobitransition metal carbonyl catalyst disclosed in claim 7 is not supported by the description and examples either (Article 6 and 33(3) PCT).
4. A catalyst cannot be immobilised and at the same time resolved or partially resolved as claimed in claim 7.

Re Item VI

Certain documents cited

- D4: XP002156527 (Comely, A.C., J. Chem. Soc., Chem. Comm., no. 4 (2000), p. 305-306)
- D5: XP002156526 (Comely, A.C., J. Chem. Soc., Chem. Comm., no. 20 (1999), p. 2075-2076)
- D6: XP002156528 (Kim, S.-W., J. Am. Chem. Soc., vol. 122, no. 7 (2000), p. 1550-1551)

Re Item VII

Certain defects in the international application

In claim 7, the wording is probably incorrect, the two possibilities being identical. Presumably, by analogy with other claims, "alkyne" is missing after "immobilised" at line 23.

Re Item VIII

Certain observations on the international application

1. Although claims 1 and 2 as well as claims 5 and 7 have been drafted as separate independent claims, they appear to relate effectively to the same subject-matter and to differ from each other only with regard to the definition of the subject-matter for which protection is sought. The aforementioned claims therefore lack conciseness (Article 6 PCT).
In order to overcome this objection, it would appear appropriate to file an amended set of claims defining the relevant subject-matter in terms of a single independent claim in each category followed by dependent claims covering features which are merely optional (Rule 6.4 PCT).
2. The term "immobilised" used in claims 1, 2, 5 and 7 is unclear since it is not described in the claims how the immobilisation is carried out (Article 6 PCT).
3. In claims 2 and 5, an immobilised alkyne transition metal carbonyl catalyst is claimed as an alternative to an immobilised transition metal carbonyl catalyst. However, the constitution of an immobilised transition metal carbonyl catalyst other than alkyne transition metal carbonyl catalyst is not clear (Article 6 PCT).
4. In claim 7, a process for the preparation of a **resolved or partly resolved** cyclopentenone compound or analogue thereof by reaction of an alkyne, an alkylene and carbon monoxide in the presence of a **resolved or partially resolved immobilised** heterobitransition metal carbonyl catalyst is disclosed.

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/GB00/03192

However, the expression "resolved or partly/partially resolved" is not clear since the reaction solvent is not mentioned in the claims (Article 6 PCT).

In addition, the fact that the catalyst should be immobilised and at the same time resolved or partially resolved leads to an inconsistency between these features, rendering the claim unclear (Article 6 PCT).

5. The variables x and m used on page 8, lines 19 and 20 and on page 9, line 5 have not been defined (Article 6 PCT).

PATENT COOPERATION TREATY

10/069356

PCT

From the INTERNATIONAL BUREAU

**NOTICE INFORMING THE APPLICANT OF THE
COMMUNICATION OF THE INTERNATIONAL
APPLICATION TO THE DESIGNATED OFFICES**

(PCT Rule 47.1(c), first sentence)

To:

BROWN, Andrew, Stephen
AstraZeneca
Global Intellectual Property
Alderley Park, P.O. Box 272
Mereside
Macclesfield, Cheshire SK10 4GR
ETATS-UNIS D'AMERIQUE

Date of mailing (day/month/year) 08 March 2001 (08.03.01)		IMPORTANT NOTICE	
Applicant's or agent's file reference PHM.70582/WO			
International application No. PCT/GB00/03192	International filing date (day/month/year) 21 August 2000 (21.08.00)	Priority date (day/month/year) 27 August 1999 (27.08.99)	
Applicant ASTRAZENECA AB et al			

1. Notice is hereby given that the International Bureau has communicated, as provided in Article 20, the international application to the following designated Offices on the date indicated above as the date of mailing of this Notice:
AU, KP, KR, US

In accordance with Rule 47.1(c), third sentence, those Offices will accept the present Notice as conclusive evidence that the communication of the international application has duly taken place on the date of mailing indicated above and no copy of the international application is required to be furnished by the applicant to the designated Office(s).

2. The following designated Offices have waived the requirement for such a communication at this time:

AE, AG, AL, AM, AP, AT, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EA, EE, EP, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, OA, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW
The communication will be made to those Offices only upon their request. Furthermore, those Offices do not require the applicant to furnish a copy of the international application (Rule 49.1(a-bis)).

3. Enclosed with this Notice is a copy of the international application as published by the International Bureau on 08 March 2001 (08.03.01) under No. WO 01/16058

REMINDER REGARDING CHAPTER II (Article 31(2)(a) and Rule 54.2)

If the applicant wishes to postpone entry into the national phase until 30 months (or later in some Offices) from the priority date, a demand for international preliminary examination must be filed with the competent International Preliminary Examining Authority before the expiration of 19 months from the priority date.

It is the applicant's sole responsibility to monitor the 19-month time limit.

Note that only an applicant who is a national or resident of a PCT Contracting State which is bound by Chapter II has the right to file a demand for international preliminary examination.

REMINDER REGARDING ENTRY INTO THE NATIONAL PHASE (Article 22 or 39(1))

If the applicant wishes to proceed with the international application in the national phase, he must, within 20 months or 30 months, or later in some Offices, perform the acts referred to therein before each designated or elected Office.

For further important information on the time limits and acts to be performed for entering the national phase, see the Annex to Form PCT/IB/301 (Notification of Receipt of Record Copy) and Volume II of the PCT Applicant's Guide.

The International Bureau of WIPO 34, ch. min des Colombettes 1211 Geneva 20, Switzerland	Authorized officer J. Zahra
Facsimile No. (41-22) 740.14.35	Telephone No. (41-22) 338.83.38

Continuation of Form PCT/IB/308

**NOTICE INFORMING THE APPLICANT OF THE COMMUNICATION OF
THE INTERNATIONAL APPLICATION TO THE DESIGNATED OFFICES**

Date of mailing (day/month/year) 08 March 2001 (08.03.01)	IMPORTANT NOTICE
Applicant's or agent's file reference PHM.70582/WO	International application No. PCT/GB00/03192

The applicant is hereby notified that, at the time of establishment of this Notice, the time limit under Rule 46.1 for making amendments under Article 19 has not yet expired and the International Bureau had received neither such amendments nor a declaration that the applicant does not wish to make amendments.

CODE	DATE	NTD
REC'D 23 MAR 2001 GIPS		
DATA ENTERED <i>WMS</i> F.L.		
FINAL CHECK <i>LCF</i>		

PATENT COOPERATION TREATY

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

Commissioner
 US Department of Commerce
 United States Patent and Trademark
 Office, PCT
 2011 South Clark Place Room
 CP2/5C24
 Arlington, VA 22202
 ETATS-UNIS D'AMERIQUE

in its capacity as elected Office

Date of mailing (day/month/year) 02 May 2001 (02.05.01)	
International application No. PCT/GB00/03192	Applicant's or agent's file reference PHM.70582/WO
International filing date (day/month/year) 21 August 2000 (21.08.00)	Priority date (day/month/year) 27 August 1999 (27.08.99)
Applicant COMELY, Alex, Christian et al	

1. The designated Office is hereby notified of its election made:

☒ in the demand filed with the International Preliminary Examining Authority on:

23 February 2001 (23.02.01)

☐ in a notice effecting later election filed with the International Bureau on:
2. The election ☒ was
☐ was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No.: (41-22) 740.14.35	Authorized officer <p style="text-align: center;">Juan Cruz</p> Telephone No.: (41-22) 338.83.38
--	--

INTERNATIONAL SEARCH REPORT

International Application No

PCT/GB 00/03192

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C07B37/10 C07B41/06

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07B C07D

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

CHEM ABS Data, BEILSTEIN Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	J. L. SPITZER: "Polymer-supported synthesis as a tool for improving chemoselectivity: Pauson-Khand reaction" TETRAHEDRON, (INCL TETRAHEDRON REPORTS), vol. 53, no. 20, 1997, pages 6791-6808, XP004105664 OXFORD GB schemes 1 and 2; table 1 --- -/--	1,2,5,7

☒ Further documents are listed in the continuation of box C.

☐ Patent family members are listed in annex.

* Special categories of cited documents :

A document defining the general state of the art which is not considered to be of particular relevance

E earlier document but published on or after the international filing date

L document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

O document referring to an oral disclosure, use, exhibition or other means

P document published prior to the international filing date but later than the priority date claimed

T later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

X document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

Y document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

& document member of the same patent family

Date of the actual completion of the international search

4 January 2001

Date of mailing of the international search report

23/01/2001

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

Wright, M

INTERNATIONAL SEARCH REPORT

Inter. Appl. Application No
PCT/GB 00/03192

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	W. A. SMIT: "New route to the synthesis of polycyclic compounds based on a stepwise AdE-reaction of dicobalt octacarbonyl complexes of conjugated enynes with a subsequent intramolecular Khand-Pauson type reaction" TETRAHEDRON LETTERS, vol. 27, no. 11, 1986, pages 1241-1244, XP002156524 OXFORD GB page 1243	1,2,5,7
A	S. O. SIMONIAN: "Adsorption effects on the efficiency of cobalt-mediated cyclizations of allylpropargyl ethers into derivatives of 3-oxabicyclo[3.3.0]oct-5-en-7-one" TETRAHEDRON LETTERS, vol. 27, no. 11, 1986, pages 1245-1248, XP002156525 OXFORD GB page 1246 -page 1247	1,2,5,7
P,X	A. C. COMELY: "Polymer-supported cobalt carbonyl complexes as novel solid-phase catalysts of the Pauson-Khand reaction" JOURNAL OF THE CHEMICAL SOCIETY, CHEMICAL COMMUNICATIONS, no. 4, 21 February 2000 (2000-02-21), pages 305-306, XP002156527 LETCHEWORTH GB the whole document	1-6
P,A	A. C. COMELY: "Polymer supported cobalt carbonyl complexes as novel traceless alkyne linkers for solid-phase synthesis" JOURNAL OF THE CHEMICAL SOCIETY, CHEMICAL COMMUNICATIONS, no. 20, 21 October 1999 (1999-10-21), pages 2075-2076, XP002156526 LETCHEWORTH GB the whole document	1,2,5,7
P,A	SANG-WOOK KIM: "Cobalt on mesoporous silica: the first heterogeneous Pauson-Khand catalyst" JOURNAL OF THE AMERICAN CHEMICAL SOCIETY, vol. 122, no. 7, 23 February 2000 (2000-02-23), pages 1550-1551, XP002156528 DC US the whole document	1,2,5,7